REMARKS

In response to the above-identified Office Action ("Action"), Applicants traverse the Examiner's rejection of the claims and seek reconsideration thereof. Claims 22-57 are pending in the present application. Claims 22-37 and 39-41 remain withdrawn. Claims 38 and 42-57 are rejected. In this response, claims 38 and 57 are amended, no claims are cancelled and claims 58 and 59 are added.

I. Claim Amendments

Applicants respectfully submit herewith amendments to claims 38 and 57. Claims 58 and 59 are new. Claim 38 is amended to correct a typographical error. Claim 57 is amended to delete the recitation of "or the prevention" to place the claim in compliance with 35 U.S.C. §112 as discussed below. New claims 58 and 59 recite that human protein kinase C beta 1 (PKC beta-1) is defined by the sequence of Genbank accession number X06318. Applicants respectfully submit the amendments and new claims are supported by the specification and do not add new matter. Accordingly, Applicants respectfully request consideration and entry of the amendments to claims 38 and 57 and newly added claims 58 and 59.

II. Claim Rejections – 35 U.S.C. §112

In the Action, claims 38, 42 and 46-57 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description and/or enablement requirement.

The Examiner alleges that in the absence of a sequence restriction for PKS beta 1, the claims cover any protein kinase (PKC) beta 2 protein or even any protein with a PKC beta 1 activity and that the application and the prior art only describe a limited number of sequences of protein kinase C beta 1. See Action, page 5, paragraphs 2-3. On this basis, the Examiner alleges that the application and prior art references do not provide enough description of oligonucleotides capable of hybridizing with protein kinase C beta 1 in general.

Applicants respectfully disagree with the Examiner's allegations. Indeed, the Examiner appears to be suggesting that the term "protein kinase C beta 1" is not understood to those of

ordinary skill in the art and does not have an ordinary meaning. This is not the case. In contrast, the family of protein kinase C isozymes were already well known and characterized at the time the Application was filed and the meaning of the term "protein kinase C beta 1" would have been understood by one of ordinary skill in the art.

This fact is clearly illustrated by, for example, an article by Hug et al. ("Hug") attached herewith which was published in 1993, well before the filing date of the application. Although this article is primarily directed to signal transduction, it summarizes the organization of the family of protein kinase C isozymes. In particular, Table 1 displays for various PKC isozymes the species in which a corresponding cDNA has been isolated and sequenced. As is evidenced by Hug, for PKC beta 1, rat, human and rabbit cDNAs had been identified. This article therefore clearly demonstrates that the name "protein kinase C beta 1" was recognized as referring to a particular protein with a known nucleotide sequence for three mammalian species about ten years before the filing date of the application.

Since then, nucleotide sequences of corresponding protein kinase C beta 1 have been identified in other species, such as chickens (gallus gallus), dogs (canis lupus familiaris), and rhesus monkeys (macaca mulatta). This is evidenced by the print out from the NCBI Entrez Gene website (www.ncbi.nlm.nih.gov/sites/entrez) attached herewith in which 12 PKC beta 1 gene references are listed.

Applicants respectfully submit when the sequence of a particular gene is known in a few species, it is only routine procedure for a skilled artisan to isolate corresponding sequences in further species, or to identify allele variants. In the present Application, it was found that down regulation of PKC beta 1 inhibits melanogenesis in melanocytes. Applicants believe that in view of the foregoing Applicants should not be prevented from obtaining a claim which is not restricted to a particular sequence.

In addition, Applicants have added new claims 58 and 59 to clarify that in some embodiments, PKC beta 1 is limited to the sequence described in Genbank accession number X06318.

Applicants believe for at least the foregoing reasons, the claims are in compliance with the written description requirement under 35 U.S.C. §112, first paragraph.

In addition, in regard to claim 57, the Examiner alleges the Application does not enable a method of prevention as recited in claim 57. In an effort to expedite prosecution of the Application, Applicants have amended claim 57 to recite a method for treatment, rather than treatment or prevention. Applicants believe the amendment to claim 57 places claim 57 in compliance with 35 U.S.C. §112.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 38, 42 and 46-57 under 35 U.S.C. §112.

III. Claim Rejections – 35 U.S.C. §102

In the Action, claims 38 and 42-57 are rejected under 35 U.S.C. §102(b) as being anticipated by International Publication No. WO 95/02069 issued to Bennett et al. ("Bennett") as evidenced by *The Use of Antisense Strategy to Modulate Human Melanogenesis* by Lazou et al. ("Lazou").

It is axiomatic to a finding of anticipation that each and every element of the rejected claim be found within a single prior art reference.

In regard to independent claims 38 and 57, Applicants respectfully submit that Bennett as evidenced by Lazou fails to teach methods for depigmenting or bleaching human skin and/or hair and for treatment of regional hyper-pigmentation, accidental hyper-pigmentation and leucodermias including the topical application of a composition "comprising at least one oligonucleotide containing between 7 and 25 nucleotides, capable of specifically hybridising with genes or gene products coding for protein kinase C beta-1 (PKC beta-1)" as recited in claims 38 and 57.

The Examiner alleges that while implementing a method as described in claims 37-53 or 70-94 of Bennett, a skilled person would necessary obtain a depigmenting effect (as allegedly

evidenced by Lazou) and thus perform a method according to claims 38 and 42-56 of the present application and that such methods are thus inherently taught in Bennett.

The same reasoning is applied by the Examiner in rejecting claim 57 directed to the treatment of particular pigmentation disorders.

Applicants respectfully disagree with the Examiner's analysis of the prior art for at least the following reasons.

A. Claims 37-58 of Bennett are directed to modulation of PKC expression

In rejecting the claims, the Examiner first relies on the method recited in claims 37-53 of Bennett. This portion of Bennett relates to a method of modulating the expression of PKC in cells in which the cells are contacted with an oligonucleotide specifically hybridizable with a PKC gene or PKC mRNA.

Specifically, the Examiner alleges that claim 48 teaches that the gene or mRNA encodes PKC beta and claim 49 specifies various sequences of possible oligonucleotides, including SEQ ID NO: 28, which is identical to SEQ ID NO: 1 of the present Application and specifically hybridizes with PKC beta 1. Thus, claim 49 relates to a method using an oligonucleotide specifically hybridizable with PKC beta 1 gent or mRNA.

These claims, however, are only directed to the modulation of PKC expression in cells. As explained in the description, "modulation" should be understood as either increasing or decreasing the expression of PKC, while only an inhibition of PKC beta 1 expression results in a depigmenting effect. Thus, the method of claim 49 of Bennett does not necessary result in a depigmenting effect.

In addition, the cells in which the expression of PKC beta 1 is modulated are not defined more precisely. As explained in the present Application, PKC beta 1 is expressed in many cells. However, a depigmenting effect can only be obtained if the antisense oligonucleotide is contacted with melanocytes. These particular cells are not cited in Bennett as particular targets of the methods according to claims 37-53, and claim 49 in particular.

Thus the method of claim 49 of Bennett fails to expressly or inherently disclose the claimed method for depigmenting or bleaching human skin or hair by topically applying the claimed cosmetic composition which includes an oligonucleotide capable of specifically hybridizing with genes or gene products coding for PKC beta-1.

B. Claims 70-94 of Bennett

The Examiner also refers to claims 70-94 which allegedly relate to a method of treating a condition associated with expression of PKC using an oligonucleotide specifically hybridizable with a PKC gene or PKC mRNA.

Claims 72 and 76 recite that the condition may be psoriasis or skin cancer respectively, and claims 89 and 90, which only depend on the general method and not on claims 72 or 76, indicate that PKC is PKC beta and that the oligonucleotide sequence may be SEQ ID NO: 28, which is identical to SEQ ID NO: 1 of the present Application.

First, Applicants wish to highlight that only claim 90 relates to a method of treating a PKC associated condition using a PKC beta 1 specifically hybridizable oligonucleotide. See Bennett, Table 3 page 26 showing that SEQ ID NO: 25 to 29 are specific for PKC beta 1.

Furthermore, the use of an oligonucleotide specifically hybridizable with PKC beta 1 is never explicitly disclosed in connection with the treatment of psoriasis or skin cancer.

Indeed, as mentioned before, claims 89 and 90 depend on claim 70, which relates to any PKC associated condition, and not on claims 72 or 76 relating more specifically to psoriasis and skin cancer.

As detailed in Bennett (see page 4 line 8-10) and in Hug (see page 330, left column lines 3-5), the PKC family includes a great number of distinct isoforms, with various biological properties and expression patterns.

As a result, each particular isoform (or isozyme) is deemed to be associated with distinct particular PKC associated conditions. From what is described in Bennett, a skilled artisan would thus not be able to conclude that an oligonucleotide specifically hybridizable with PKC beta 1

(i.e. an antisense oligonucleotide inhibiting PKC beta 1 expression) might be useful for treating specifically psoriasis or skin cancer.

In contrast, in the description of Bennett, it is indicated that in psoriatic lesions, there is an alteration on the ratio between PKC-α and PKC-β, with a preferential loss of PKC-β compared to normal skin. See Bennett, page 4 lines 11-15.

Thus, it appears that psoriasis is associated with a decrease of PKC-β expression and that an antisense oligonucleotide to PKC beta 1, which would further decrease the expression of PKC beta, would be more detrimental than useful in the treatment of psoriasis.

In addition there is no indication in Bennett that a decrease of PKC-beta 1 would be beneficial in the treatment of skin cancer.

Globally, it is thus clear that Bennett does not disclose or suggest a specific method of treating psoriasis or skin cancer with an antisense oligonucleotide specific for PKC beta 1. In the case of psoriasis, the teachings of Bennett teach away from the use of an antisense oligonucleotide specific for PKC beta 1 in psoriasis treatment.

For at least the reasons that a method of treating psoriasis or skin cancer using an antisense oligonucleotide to PKC-beta 1 is not disclosed, an inherent bleaching effect is further not disclosed in Bennett.

Applicants further wish to draw the Examiner's attention to the fact that, although the claims of Bennett are generally directed to PKC, all experimental results concerning potential therapeutic use of PKC antisense oligonucleotides displayed in Bennett only relate to PKC-α. See Bennett, Examples 9-12. Indeed, although antisense oligonucleotides specific for PKC beta 1 and/or 2 are disclosed, absolutely no therapeutic use of these oligonucleotides is supported in Bennett. The generalization that oligonucleotides specific for PKC beta might have any therapeutic effect is thus purely speculative.

In addition, none of the described experimental results actually relate to psoriasis or skin cancer. The therapeutic use of any PKC isoform antisense oligonucleotide for treating psoriasis or skin cancer is thus also purely speculative.

There is no real teaching in Bennett that an antisense oligonucleotide to PKC of any isoform might be used for treating psoriasis or skin cancer, and even more, no teaching that an antisense oligonucleotide of PKC beta 1 should be used.

C. Claim 90 of Bennett

Finally, concerning claim 57, even if the Examiner considers that claim 90 discloses a method of treating psoriasis or skin cancer using a PKC-beta 1 specific antisense oligonucleotide, which is not the case for the reasons previously discussed, it would not disclose a method for treating the selected pigmentation disorders of claim 57. Indeed, the oligonucleotide would be contacted with skin areas affected by psoriasis or skin cancer, but not by the particular disorders recited in claim 57.

Thus, for at least the foregoing reasons, Bennett fails to teach each and every element of claims 38 and 57. Since each of the elements of the claims are not found within the cited prior art, claims 38 and 57 are not anticipated by the cited prior art reference. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 38 and 57 under 35 U.S.C. §102 over Bennett as evidenced by Lazou.

In regard to claims 42-56, these claims depend from claim 38 and incorporate the limitations thereof. Thus, for at least the reasons that claim 38 is not anticipated by Bennett, claims 42-56 are further not anticipated by the cited prior art reference. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 42-56 under 35 U.S.C. §102 over Bennett as evidenced by Lazou.

IV. New Claims 58 and 59

In regard to new claims 58 and 59, these claims depend from claims 38 and 57, respectively, and incorporate the limitations thereof. Thus, for at least the reasons that claims 38

and 57 are not anticipated by the cited prior art references, claims 38 and 59 are further allowable over the prior art. Applicants respectfully request reconsideration and allowance of claims 38 and 59 at the Examiner's earliest convenience.

CONCLUSION

In view of the foregoing, it is believed that all claims now pending are in condition for allowance and such action is earnestly solicited at the earliest possible date. If there are any additional fees due in connection with the filing of this response, please charge those fees to our Deposit Account No. 02-2666. Questions regarding this matter should be directed to the undersigned at (310) 207-3800.

Respectfully submitted,

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CERTIFICATE OF TRANSMISSION

I hereby certify that this correspondence is being submitted electronically via EFS Web to the United States Patent and Trademark Office on May 5, 2008.

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